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Depression among Tuberculosis Patients and its Association with Medication Adherence of Anti-Tuberculosis Drugs: Literature Review

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ABSTRACT

Introduction: Tuberculosis or known as TBC is one of communicable disease that caused by the bacillus Mycobacterium tuberculosis. This disease is the major of public health problem due to it can spread easily from the patients to the healthy people by air transmission. In order to stop the transmission and improve the health status of the community, treatment is needed for patients with tuberculosis. But, almost people with tuberculosis patients had poor treatment and the factor that contribute to their adherence is depression. Depression and tuberculosis are frequently coexisting in individuals. Depression lead them having negative perception about the treatment and get misconceptions about TB disease. Therefore, most of tuberculosis patients with depression are having lower level of medication adherence.

Objective: The purpose of this literature review is to analyze the association between depression among tuberculosis patients with medication adherence of anti-tuberculosis.

Method:.This study uses the literature review method to review the results of research that has been published by previous researchers. The literature sources obtained were the results of searches from three online databases, namely Google scholars, Pubmed, and Scopus. which published in the range of 2018-2024.

Result: Depression was significantly associated with medication adherence among people who had tuberculosis

Conclusion: Depression appears to be a strong risk factor for treatment failure and default in these people with newly diagnosed tuberculosis and is associated with poor treatment outcome despite successful tuberculosis treatment. This could be happened because of long period time that needed to consume the treatment and complexity of the drug regimen.

Keywords: Depression; Medication Adherence; Tuberculosis

INTRODUCTION

Tuberculosis or known as TBC is one of communicable disease that caused by the bacillus Mycobacterium tuberculosis. It can be spread easily from patients suffering from pulmonary TB to healthy people by air transmission as like coughing. World Health Organization (WHO) reported that TB is the cause of illness for around 10 million people every year and has been ranked among the top ten causes of death globally (1). Based on data report in 2022, Tuberculosis case in Indonesia ranked the second place after India with 969.000 cases and 93.000 deaths per year or equivalent to 11 deaths per hour (2). It indicates that population in Indonesia are very vulnerable to transmit the disease. In order to stop the transmission and improve the health status of the community, treatment is needed for patients with tuberculosis.

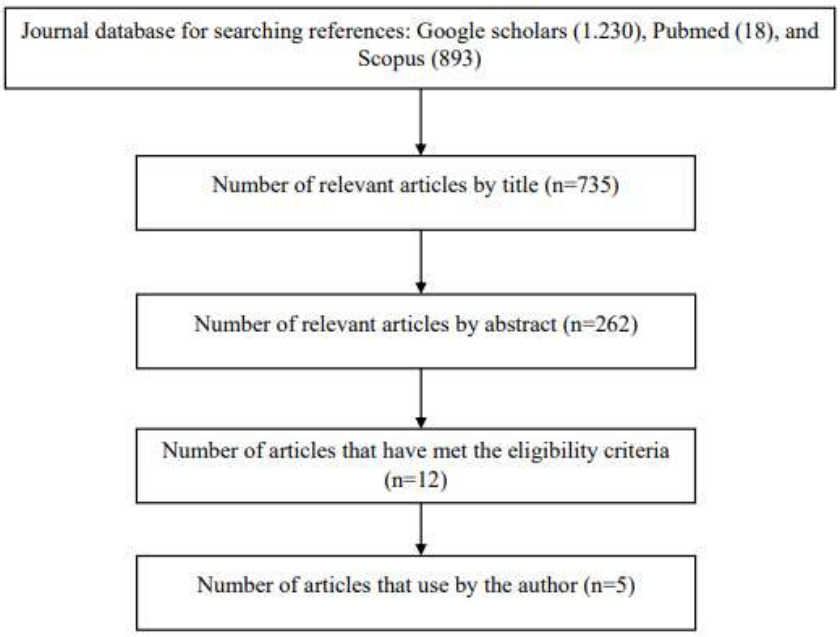
Without treatment, the death rate from TB disease is high (about 50%). That's why, anti-TB drug treatment is required for TB patients to cure the disease and prevent disease transmission. Comparable to other complex diseases, TB patients have to be treated with several drugs for a long period(3). According to the WHO guideline, active pulmonary TB patients should take drugs for at least 6 months, while latent tuberculosis infection (LTBI) patients should take drugs for at least 3 months. The treatment duration can be extended if TB patients are diagnosed as multi-drug resistant tuberculosis (MDR-TB), a resistance of the pathogen to the most potential anti-TB medicine. MDR-TB treatment can be up to 24 months using multiple drugs (4).

The high incidence of pulmonary TB disease in the world, especially in Indonesia, raises problems such as long and complex therapy, disease complications and many other concerns that can trigger depression. Pulmonary TB requires treatment for a long time, so people with pulmonary TB will be feeling bored to consume those drugs everyday and very likely to experience depression (5). Depression is a common mental disorder characterized by persistent sadness, lack of interest in activities, reduced energy, vegetative symptoms, suicidal ideation and causing levels of social and occupational dysfunction (6). Depression often makes a person lose interest or motivation, causes feelings of hopelessness and leads to drastic mood changes, such as feelings of deep sadness, irritability or loss of hope.

Depression and tuberculosis are frequently coexisting in individuals. They also usually share common risk factors that make high prevalence of comorbidity with estimates ranging from 10-52% across studies (7). Besides that, study in China reported that there was significant association between depressive symptoms and medication adherence in patients with tuberculosis, which depression can affect one's willingness and ability to adhere to the treatment plan (8). Depression also lead them having negative perception about the treatment and get misconceptions about TB disease. They assume that TB is a dangerous disease that has a low chance of survival and little hope of recovery. As a result, many TB patients discontinue their treatment and having low motivation to be healthy (9). Beside that, they are often neglected by people around them because if long term drug treatment due to the nature of diasease or tend to be avoided by those around them due to the infectiousness of TB so the patients would feel alone and unwanted to live (10). Thus, it is important to provide positif support to people who had tuberculosis and make them realize to care about their helath and never had prolonged negative thoughts. The purpose of this study is to analyze the association between depression and medication treatment and also the impact of depression on people with tuberculosis.

METHOD

This study uses the literature review method to review the results of research that has been published by previous researchers. The literature sources obtained were the results of searches from two online databases, namely Google scholars, Pubmed, and Scopus. The selection of literature was based on the inclusion criteria which included articles using Indonesian and English, articles published in the range of 2018-2024, and article searches using the keywords "medication adherence", "depression", and "tuberculosis".



RESULTS

Based on the results of the article search, five articles were found that fit the topic and met the inclusion criteria. The results of the review conducted by the author are presented in table 1.

Table 1. Result of Literature Review

Authors (Year)	Article	Purpose	Method	Result
Abdul Rouf, Muneer A. Masoodi, Mohammad Maqbool Dar, S. Mohammad Salim Khan, Rubeena Bilquise (2021).	Depression among Tuberculosis Patients and its association with treatment aoutcomes in district Srinagar.	The purpose of this research is to analyze the association between depression with treatment outcomes among tuberculosis patients	This research is using prospective study that was conducted in Srinagar District, India and it need one and a half years tsarting from 1st April 2017 to 30th September 2018. The partisipants here were 202 adults over 18 years old with newly diagnosed TB. Data collection was done at three time-points: baseline (within one month of anti-TB treatment), after 2 months (end of intensive phase) and after 6 months (end of continuation phase).	Based on the research showed that depression in TB patients was associated with negative treatment outcomes (treatment failure and default) and the strength of association was estimated to be small to medium. Depression appears to be strong risk factor for treatment failure and is associated with poor tertamnet outcome despite successful tuberculosis treatment. Based on the prevalence of depression, we can know that the prevalence of patients who had depression at baseline was 50,50%, depression after 2 months was 9,40%, and depression after 6 months was 2,74%. It indicates that most of patients were having high depression at baseline level. Low incidence of depression at 2 months dan 6 months during the anti-TB treatment

				seem to be because of the protective effect of anti-TB treatment and feeling of wellbeing by the patients. On another hand, this study revealed that patients who responded to counselling, psychoeducation or antidepressants given in few patients (Depression with suicidal ideation) in the intensive phase of anti-TB treatment had good treatment outcome in majority of patients possibly due to better adherence. But, after 2 months of anti-TB treatment the strength of association between depression and worst treatment outcome increase and those patients who remained depressive for more than 2 months after treatment had 59 times risk of treatment failure than those without depression.
Dinesh Panati, Chandra Sekhar Chittooru, Yethi Raju Madarapu, Ananda Krishna Gorantla (2023).	Effect of depression on treatment adherence among elderly tuberculosis patients: A prospective interventional study	The purpose of this research is to estimate prevalence of depression and medication adherence in elderly patients with tuberculosis and its association. On another hand, it also observed the change of treatment adherence after giving management of depression.	This research is using prospective interventional study with cross sectional design. This Study was conducted at the District Tuberculosis Centre (DTC), Chittoor, Andhra Pradesh, India and it was carried from January 2022 to September 2022. The total of participants here were 100 patients who diagnosed with tuberculosis under 60 years old, registered at and taking DOTS within the last one month.	Based on the research showed that depression was associated with medication adherence among elderly patient tuberculosis which almost one in every two elderly tuberculosis patients do suffer from depression and around 90% have to low to moderate treatment adherence. Based on the data, we can see that there were 55 participants who had depressed and just 45 participants who had normal depression status during their treatment. Regression analysis was also carried to find out the predictors for low to medium adherence with medication. Among various variables assumed to predict low to medium adherence with medication, depression was the only significant predictor for low to medium adherence with medication and is found to have 43.6 times risk for low to medium adherence with

				medication. Beside of that, with intervention of depression, the risk of low to medium adherence was reduced by 50,9% from 90,9%. It can happen because after intervention of depression, the patients started to change their treatment to be better. Patients who developed depression after two months of the intensive period still had good treatment outcomes as they responded to depression quickly and had no depression after 6 months of anti-TB treatment.
Fentie Ambaw, Rosie Mayston, Charlotte Hanlon, Girmay Medhin, Atalay Alem (2018).	Untreated depression and tuberculosis treatment outcomes, quality of life and disability, Ethiopia	The purpose of this research is to investigate the association between comorbid depression and tuberculosis treatment outcomes, quality of life and disability in Ethiopia	This research is using prospective observational study that was conducted in December 2014 and July 2016. The study involved 648 consecutive adults treated for tuberculosis at 14 primary health-care facilities in south central and northern Ethiopia. All were assessed at treatment initiation (i.e. baseline) and after 2 and 6 months.	Based on the research showed that after 6 months the treatment default rate was significantly higher among participants with probable despression at baseline (3,9%) than among those without (0,8%). Similarly, the proportion who had died was significantly higher among those with probable depression (7,8%) than without (1,9%). But, the treatment success rate was significantly lower in those who with probable depression (87,7%) than without (96,6%). This study also provides evidence that people with tuberculosis in Ethiopia who had probable depression at the start of treatment were significantly more likely to default on treatment or die. Moreover, probable depression was also associated with poorer quality of life and greater disability which happened at the start and after completion of antituberculosis treatment. In Ethiopia, comorbid of depressive symptoms in people with tuberculosis are usually associated with negative outcomes,

				eventhought they were included in successful treatment category. As the result, unnoticed comorbid depressive symptoms can hamper efforts to end tuberculosis and affect the medication adherence.
Lionel Che Anye, Marie Ebob Agbortabot Bissong, Anna Longdoh Njundah, Joseph Nelson Siewe Fodjo (2023).	Depression, anxiety and medication adherence among tuberculosis patients attending treatment centres in Fako Division, Cameroon: cross-sectional study.	The purpose of this research is to investigate depression, anxiety and medication adherence among Cameroonian tuberculosis patients.	This research is using cross sectional design that was conducted from 1 March to 30 June 2022 across five treatment centres in Fako Division, Southwest Region, Cameroon. The study involved 375 participants who were 21 years and above with tuberculosis diagnosed.	Based on the research showed that the prevalence of depression among tuberculosis patients was 47,4%. There were 340 patients (90,7) who adherence to their medication and 35 patients (9,3%) were'nt. From this finding, we can know that both depression and anxiety were positively associated with non-adherence of tuberculosis treatment. It can be happened because non-adherence leads to poor prognosis and thus poor treatment outcomes, leading to breakdown of the mental health of tuberculosis patients.
Paulo Ruiz Grosso, Rodrigo Cachay, Adriana de la Flor, Alvaro Schwalb, Cesar Urgante Gil (2020)	Association between tuberculosis and depression on negative outcomes of tuberculosis treatment: A systematic review and meta-analysis	The purpose of this study is to reviewed studies that evaluates depressive symptoms directly or indirectly through psychological distress (PD) and measured negative treatment outcomes of drug-sensitive pulmonary TB, defined as death, loss to follow-up, or non-adherence.	This research is using systematic review and the database was from Pubmed, Global Helath library, Embase, Scopus and Web of Science for English language article publich anytime up to 9th of August 2019.	Based on the research showed that across eight studies, depressive symptoms are significantly associated with death and loss to follow-up during TB treatment (OR = 4.26). In addition, the combination of depressive symptoms (DS) and psychological distress (PD) also significantly increases the odds of negative TB treatment outcomes (OR = 4.05). Neither DS nor PD appear to be associated with non-adherence during TB treatment (OR = 1.34).

DISCUSSION

Depression and tuberculosis are related each other. The increase in pro-infammatory cytokines associated with depression reduces activation of the cellular and humoral immune systems, which contributes to tuberculosis progression. Similarly, tuberculosis infection can cause chronic infammation by releasing pro-infammatory cytokines that stimulate enzymes in the central nervous system, and some anti-TB medications may contribute to mental health issues such as depression. Comorbid depression and tuberculosis can result in poor quality of life, non-adherence to anti-TB medications, progression to Multi Drug Resistant TB, and even death from the disease (11). The prevalence of depression in TB patients is repotedly more than 3 times higher than in "healthy" patients without TB (12).

Based on several studies which have been reviewed above it can be concluded that depression was significantly associated with medication adherence among people who had tuberculosis (13–16). Most of the patients with depression have low adherence to medication. A study in China supported this and stated, patients with a low adherence were significantly more depressed than patients with medium adherence, and patients with medium adherence were significantly more depressed than patients with high adherence (8). This indicates that patients with depression are not adequately adherent to medication, which in turn worsens the outcome of tuberculosis. This could be happened because of long period time that needed to consume the treatment and complexity of the drug regimen. Usually, the longer patients consumed anti-TB, the worst their medication adherence (17,18). However, it seems to be different with study from Srinagar District which said the prevalence of patients who had depression at baseline was 50,50%, depression after 2 months was 9,40%, and depression after 6 months was 2,74% (14). It indicates that most of patients were having high depression at baseline level. Many responses occurred at the beginning of the treatment such as bored, feeling pressured to take the medicine everyday which it will be faced for the next 6 months, worried about the stigma from the community and also the side effect of the drugs. Generally, in the early stage of the treatment, the patients would get the effect of the drugs that caused dizziness, reddish urine, chest palpitations and sleeplessness which sometimes disturb patient's daily activity and also caused anxiety disorders (19). But, the patients who was used to consumed the drugs would started to feel better psychologically cause they know the consequent

Another study in Ethiopia also showed that the patients who had probable depression at the start of treatment were significantly more likely to default on treatment or die. Moreover, their chance of successful treatment was lower. In this study found that people with depression may increase mortality through decreased self-care including failure to take medications and the fact that there were 113 of 648 study participants reported suicidal ideation (20). From that data, we can see that patients who had poor medication adherence and depression would be in danger situation if not treated immediately. The way of intervention that should be given is treating the psychological aspects of TB which may lead to better clinical outcomes. Psychotherapy during TB treatment was found to be leading to higher adherence, treatment, and cure rates in a prospective controlled trial in India. Psychological support as an intervention can improve treatment adherence and completion. Counselling and psycho-education was done in all TB patients irrespective of their depression status to avoid the intervention bias and only those patients with suicidal ideation were given anti-depressants drugs by the Consultant Psychiatrist (14). This also supported by previous study showed after getting intervention, the prevalence of low to medium adherence was reduced from 90.9% to 40% and compared to before intervention was 50,9% (13). It really proved that psychological intervention for tuberculosis patients is important aspects to consider during the tuberculosis treatment process, may improve patients' mood and increase medication adherence of their treatment.

CONCLUSION

In summary, the result of all literature review showed that depression was significantly associated with medication adherence among tuberculosis patients. Patients with low level adherence were significantly more depressed than patinets who had high level adherence. Long period of consuming the drugs, complexity of the regimen, side effect of the drugs, stigma from the community, also sense of boredom contributes in reducing medication adherence in tuberculosis patients. In addition, depression appears to be a strong risk factor for treatment failure and default in these people with newly diagnosed tuberculosis and is associated with poor treatment outcome despite successful tuberculosis treatment. However, depression in tuberculosis patients can be improved by psychotherapy intervention such as counseling and pyscho-education to make better medication adherence.

SUGGESTION

It is essential to know in-depth factors that influence depression in tuberculosis patients, especially pulmonary tuberculosis. As the result, it can be a reference for health workers, families, and the community to provide support for tuberculosis patients and not to fall into depression.

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